REMARKS

I. Overview

Applicants hereby request an interference between Applicants' U.S. Application Serial No. 10/789,678 ("the '678 application") and United States Patent No. 6,682,702 ("the '702 patent") which issued to Barth *et al.* on January 27, 2004. Applicants have satisfied the requirements of 35 U.S.C. §135(b)(2) by filing a preliminary amendment dated February 27, 2004, copying claims 1-48 of the Barth 2003/0040011 Application. The claims were copied before one year after the date on which the Barth 2003/0040011 Application claims were published. Moreover, 35 U.S.C. §135(b)(1) does not bar Applicants from filing this Request because the Barth 2003/0040011 published application claims 1-48 are identical to the '702 patent claims 1-48.

To facilitate consideration of this request, Applicants attach a proposed PTO-850 "Interference Initial Memorandum" outlining the suggested interference.

37 C.F.R. § 41.202 requires a suggestion for interference to:

- (1) Provide sufficient information to identify the application or patent with which the applicant seeks an interference,
- (2) Identify all claims the applicant believes interfere, propose one or more Counts, and show how the claims correspond to one or more Counts,
- (3) For each Count, provide a claim chart comparing at least one claim of each party corresponding to the Count and show why the claims interfere within the meaning of § 41.203(a),
- (4) Explain in detail why the applicant will prevail on priority,

10/789,678

- (5) If a claim has been added or amended to provoke an interference, provide a claim chart showing the written description for each claim in the applicant's specification, and
- (6) For each constructive reduction to practice for which the applicant wishes to be accorded benefit, provide a chart showing where the disclosure provides a constructive reduction to practice within the scope of the interfering subject matter.

II. 37 C.F.R. § 41.202(a)(1) - Identification of Patent

Applicants seek an interference with United States Patent No. 6,682,702, which issued to Barth *et al.* on January 27, 2004.

III. 37 C.F.R. §§ 41.202(a)(2) and (a)(3) – Identification of Interfering Claims, Proposed Count(s), and Claim Correspondence

A. Interfering Claims

37 C.F.R. § 41.203(a) provides as follows:

An interference exists if the subject matter of a claim of one party would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party and vice versa.

Applicants' claims 141, 143, 146-148, 151-153, 155-156, 158-159, 161, and 163 correspond exactly to the '702 patent claims 1, 8, 11-13, 17-19, 21-22, 30, 37, 43, and 47, respectively. Applicants' claims 142, 144-145, 149-150, 154, 157, 160, and 162 are substantially similar to the '702 patent claims 7, 9-10, 14, 16, 20, 23, 42, and 44, respectively. The claim chart in Appendix A compares these claims as required under 37 C.F.R. § 41.202(a)(3). Each of Applicants' claims 141-163, if prior art, would have anticipated or rendered obvious the subject matter of the '702 patent claims 1, 7-14, 16-23, 30, 37, 42-44 and 47 respectively, and vice versa. Therefore, at least these claims are believed to "interfere" within the meaning of § 41.203(a).

10/789,678

B. Proposed Count

37 C.F.R. §41.201 provides that "Count means the Board's description of the interfering

subject matter that sets the scope of admissible proofs on priority." For the purpose of the

suggested interference, Applicants propose a single Count defined as follows:

Claim 37 or 47 of the '702 patent

or

Applicants' Claim 159 or 163

As shown in § A, supra, claims 37 or 47 of the '702 patent, if prior art, would have

anticipated or rendered obvious the subject matter of Applicants' claims 159 or 163 and vice

versa (see also Appendix A). Therefore, these claims interfere within the meaning of 37 C.F.R.

§ 41.203(a) and provide an appropriate Count.

C. Correspondence of Claims to Proposed Count

Under the provisions of 37 C.F.R. § 41.207(b)(2), a claim corresponds to a Count if the

subject matter of the Count, treated as prior art to the claim, would have anticipated or rendered

obvious the subject matter of the claim.

The claims of the parties that are believed to correspond to the Proposed Count are as

follows:

Barth et al. ('702 patent):

Claims 1-49 (all)

Applicants (Besemer et al.): Claims 141-163 (all)

The claims of the parties that are believed not to correspond to the Proposed Count are as

follows:

Barth et al. ('702 patent):

none

Applicants (Besemer et al.): none

10/789,678 - 3 -

1. Designation of Barth '702 Patent Claims 1-49

Below, Applicants explain why the '702 patent claims 1-49 should be designated as corresponding to the proposed Count.

Claims 1-49 of the '702 patent each would have been anticipated or rendered obvious over the proposed Count, treating the proposed Count as prior art to these claims, and, therefore, should be designated as corresponding to the proposed Count for at least the following reasons:

Claim 1 is an independent claim which recites a method of simultaneously Claim 1. conducting multiple chemical reactions in a reaction assembly having a microtiter plate of wells containing test samples and an array of sets of chemical reactants. The claim further recites a method of assembling the array of sets of chemical reactants to the microtiter plate of test samples such that the array covers open ends in the test sample wells of the microtiter plate to form a plurality of closed cells, wherein each closed cell contains a set of chemical reactants and a respective test sample. Claim 1 further recites the steps of sealing the microtiter plate to the array to create one or more of a gas tight, a liquid tight, and a fluid tight seal and mechanically agitating the sealed reaction assembly to contact the test samples with the chemical reactants in each closed cell simultaneously. Claim 1 would have been obvious over the proposed Count in view of United States Patent No. 5,945,334 ("the '334 patent") or U.S. Patent No. 5,922,591 ("the '591 patent") which issued on August 31, 1999 and July 13, 1999, respectively. The '334 and '591 patents are both prior art references against the '702 patent under 35 U.S.C. §102(b). The present application is a continuation of the '334 patent through a series of continuation applications.

The proposed Count recites an apparatus for simultaneously conducting multiple chemical reactions having a plate with a plurality of wells spatially arranged in a surface of the

10/789,678 - 4 -

plate in a well array pattern, each well having a side wall adjacent to a closed end that enclose the well except for an open end that is opposite the closed end and that is adjacent to the plate surface. The plurality of wells in the plate receive a test sample via the open end. The proposed Count further recites an array of sets of chemical reactants wherein the sets of chemical reactants are bound to and spatially arranged on a surface of an array substrate in an array pattern of features, the well array pattern being spatially similar to the feature array pattern, wherein the array surface faces the plate surface and covers the open ends of the wells to form closed cells, each closed cell having a respective test sample and a respective set of the chemical reactants. Furthermore, the proposed Count recites a seal between the plate and the array that is one or more of gas tight, liquid tight, and fluid tight.

It was well known in the art that a microtiter plate having wells containing test samples could be mechanically agitated to mix the test sample contents with the chemical reactants and an array of chemical reactants. For example, the '334 patent discloses a chip apparatus having a plurality of cavities. Col. 18, lines 19-20. A chip or substrate wafer is mounted to the cavity forming a closed cell in the reactor apparatus. Col. 18, lines 21-25. Selected fluids are introduced into and out of the cavity via the inlets and outlets. Col. 7, lines 7-8. Next, the chip package is mounted on a vortexer (2910) to vibrate the chip apparatus, "similar to a paint mixer." Col. 19, lines 43-44. The vortexer mixes targets in the fluid with the probe arrays located on the chip, increasing the hybridization rate between the targets and complementary probe sequences. Col. 19, lines 40-50 and col. 7, lines 11-12.

Additionally, the '591 patent discloses a nucleic acid diagnostic device wherein samples are agitated by means including, *inter alia*, mechanical mixing, acoustic mixing, or optimized acoustic mixing. Col. 4, lines 35-39 and Figure 7A-7C. In particular, the '591 patent discloses a

10/789.678 - 5 -

PZT (piezoelectric) element that is contacted on the surface of the device to generate vibrations in order to mix a fluid sample in the diagnostic device. Col. 32, lines 38-57. The '591 patent also provides examples of mechanical mixing, such as vertical rotation of the device. Col. 42, lines 6-10.

Thus, in view of the proposed Count and these teachings, it would have been obvious to one of ordinary skill in the art to create an embodiment of claim 1, in which the microtiter plate is mechanically agitated in order to mix the test sample with the chemical reactants in each closed cell and thus increase hybridization between the targets and complementary probe sequences.

Therefore, claim 1 should be designated as corresponding to the proposed Count.

Claim 2. Claim 2 is dependent on claim 1 and further recites the step of placing a pliable gasket between the microtiter plate and the array, the gasket having an arrangement of through holes that align with the test sample wells and the sets of chemical reactants. Claim 2 further recites the step of sealing including applying one or more of mechanical clamps, radiation, heat, external fluid pressure, vacuum and an adhesive to the reaction assembly. Claim 2 would have been obvious over the proposed Count in view of the '334 patent.

The proposed Count recites, *inter alia*, a seal between the plate and the array that is one or more of gas tight, liquid tight, and fluid tight. It was well known in the art to use a seal or gasket having through holes. For example, the '334 patent discloses several fluid retaining seals, including gaskets or seals. Col. 16, line 49. The gasket or seal (2070) is located between the ledge of the chip apparatus and the chip substrate to ensure a tight seal around the cavity (310). Col. 16, lines 49-50. This gasket, when used in a microtiter body, would have inherently contained through holes to allow mixing of the probe and target sequences. (See description of

10/789,678 - 6 -

microtiter body at col. 18, lines 18-28). Thus, it would have been obvious to the skilled artisan to create an embodiment of claim 2, in which the seal of the microtiter plate is a gasket with through holes that align with the test samples in order to ensure a tight seal around the cavity, while concurrently allowing the test sample to effectively mix and hybridize with the probe array.

Furthermore, use of mechanical clamps, radiation, heat, external fluid pressure, or adhesives in a microtiter plate were well known in the art. For example, the '334 patent discloses the use of clamps or a frame which joins the chip substrate to a package. Col. 16, line 44 and Figure 20a. Alternatively, screws, clips or adhesives may be used to mate the chip to the package. Col. 16, lines 54-56. Moreover, the '334 patent discloses the use of ultraviolet cured silicone, cement (col. 16, line 34), adhesive films, tape (col. 16, line 40), gaskets or seals (col. 16, line 49), acoustic welding (col. 16, line 52), screws (col. 16, line 54), heat and force (col. 16, line 63-64), insert molding, wave soldering, surface diffusion, laser welding, shrink wrap, o-ring seal, surface etching, or heat staking from the top (col. 17, lines 8-11) as methods used to attach the probe array to the cartridge package. In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used mechanical clamps, radiation, heat, external fluid pressure, or adhesives in the chip package to securely mate the substrate to a chip package.

Thus, claim 2 would have been obvious over the proposed Count in view of the '334 patent and should therefore be designated as corresponding thereto.

<u>Claims 3 and 4.</u> Claim 3 is dependent on claim 2 and further recites that the gasket comprises an adhesive on at least one gasket surface that interfaces with the microtiter plate or the array, and wherein the step of scaling [sic sealing] further comprises removing one or more

10/789,678 - 7 -

of mechanical clamps, radiation, heat, external fluid pressure, and vacuum after a period of time. Claim 4 is dependent on claim 3 and further recites that the adhesive is selected from an ultraviolet (UV) light curable adhesive that has increased adhesion with the application of UV light to the adhesive, and a releasable adhesive that has reduced adhesion with the application of one or more of heat, cold and radiation to the adhesive. Claims 3 and 4 would have been obvious over the proposed Count in view of the '334 patent.

The '334 patent discloses a flow cell device having a gasket or seal (2070) which is located between the ledge of the device and the chip to ensure a tight seal around the cavity (310). Col. 16, lines 49-50. The device further includes a ridge (560) that is large enough to receive adhesives for attaching the chip to the package. The adhesive may be an ultraviolet cured silicone, cement, or other adhesive. Col. 16, line 34-35. The '334 patent describes a head unit which locates a UV light above the adhesive and cures it to harden the adhesive. Col. 15, lines 10-14. Thus, the light curable adhesive has increased adhesion with the application of UV light. The gasket, which is located next to the chip, would inherently contain adhesives on at least one surface in order to attach the chip substrate to the package. Thus, it would have been obvious to one of ordinary skill in the art to have provided an adhesive on the surface of a gasket in order to attach the chip substrate to the package and thus provide a tight seal around the cavity.

Furthermore, it was well known in the art that microtiter plates could contain a removable or releasable mechanical clamp, such as a releasable adhesive. For example, the '334 patent discloses a plurality of mechanical clamps, including, among others, clamps, frames, or tapes that comprise non-permanent adhesives. Col. 17, lines 26-27. The non-permanent tape adhesive is placed over the inlets of the flow device to be sealed or unsealed without completely

10/789,678 - 8 -

separating the tape from the package. Col. 17, lines 26-27. Thus, the removable adhesive allows for convenient sealing and resealing of the inlets without completely removing the tape. In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have provided for a removable or releasable adhesive that has reduced adhesive strength with application of heat, cold and radiation, or an ultraviolet light curable adhesive that has increased adhesive strength with the application of UV light, in order to control the strength of the adhesive and allow for convenient sealing and resealing of the device without complete removal of the adhesive.

Therefore, claims 3 and 4 would have been obvious over the proposed Count in view of the '334 patent and should be designated as corresponding thereto.

Claims 5 and 6. Claim 5 is dependent on claim 2 and further recites a gasket having at least one channel that interconnects at least two through holes, such that the reaction assembly has at least two closed cells that are interconnected, and wherein in the step of mechanically agitating, the agitation has an acceleration, and the step of mechanically agitating includes the step of incrementally increasing the acceleration to sequentially mix the test samples of the interconnected closed cells. Claim 6 is dependent on claim 5 and further recites that the interconnected closed cells are located adjacent to each other. Claims 5 and 6 would have been obvious over the proposed Count in view of U.S. Patent No. 5,100,626 ("the '626 patent) and the '334 patent. The '626 patent issued on March 31, 1992, and is a prior art reference against the '702 patent under 35 U.S.C. § 102(b).

Channels in flow devices were well known in the art. For example, the '626 patent discloses a binding assay device having a resilient gasket (16) which contains an array of parallel channels (46) for receiving multiple samples for assay. Col. 2, lines 3-6. Test samples are

10/789,678 - 9 -

introduced into the channels (46) through channel openings (62 and 58) at the termini of the closed channels. Col. 2, lines 11-14. The interconnected channel openings (62 and 58) or cells are located adjacent to each other. See Figures 3 and 4a. The use of gasket channels having channel openings is used to "reduce spillage and cross-contamination" between channels or wells in the binding assay. Col. 5, lines 13-14. Furthermore, fluid that is filled through a pipettor into either of the channel openings (62 and 58) are allowed to mix in the channel portion. Col. 5, lines 9-17 and Figures 3 through 4b. In view of the proposed Count and the '626 patent, it would have been obvious to one of ordinary skill in the art to have provided for a gasket having channels portions that allow introduction of fluid through channel openings in order to reduce spillage and cross-contamination between other channels or wells in the flow device and further to allow test samples of interconnected closed cells to mix in the channel portion of the device.

Furthermore, the step of incrementally increasing the agitation of a flow device to sequentially mix the test samples of the interconnected closed cells would have been obvious to one of ordinary skill in the art over the proposed Count in view of the '334 patent. The '334 patent discloses a chip package that is mounted on a vortexer (2910) to vibrate the chip package, "similar to a paint mixer." Col. 19, line 43-44. The vortexer mixes targets in the fluid with the probe arrays located on the chip, increasing the hybridization rate between the targets and complementary probe sequences. Col. 19, lines 40-50 and col. 7, lines 11-12. Thus, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have accelerated the speed of the vortexer because discovering the speed of agitation or other workable ranges of mechanical agitation involves only routine skill in the art.

Thus, claims 5 and 6 would have been obvious over the proposed Count and should be designated as corresponding thereto.

10/789,678 - 10 -

Claim 7. Claim 7 is dependent on claim 1 and further recites that the array is made of a flexible material and is placed against the microtiter plate using one or more of mechanical clamps, radiation, heat, external fluid pressure, vacuum and an adhesive to seal the reaction assembly. Claim 7 would have been obvious over the proposed Count in view of the '334 patent or U.S. Patent No. 5,143,854 ("the '854 patent") or U.S. Patent No. 5,429,807 ("the '807 patent"). The '854 patent issued on September 1, 1992 and the '807 patent issued on July 4, 1995. Both '854 and '807 patents are prior art references against the '702 patent under 35 U.S.C. §102(b).

The '334 patent discloses an array made from a flexible material. For example, the '334 patent discloses several materials that may be used in the construction of the substrate wafer, including, among others, "biological, nonbiological, organic, inorganic, or a combination of any of these, existing as particles, strands, precipitates, gels, sheets, tubing, spheres, containers, capillaries, pads, slices, films, plates, slides, etc." Col. 4, lines 47-51. Furthermore, the '334 patent teaches that the "the wafer may be a polymerized Langmuir Blodgett film, functionalized glass, Si, Ge, GaAs, GaP, SiO₂, SiN₄, modified silicon, or any one of a wide variety of gels or polymers such as (poly)tetrafluoroethylene, (poly)vinylidenedifluoride, polystyrene, polycarbonate, or combinations thereof." Col. 4, lines 59-64. Many of the materials listed in the '334 patent are flexible.

Additionally, the '854 patent discloses an array that is made from a material having a semi-rigid surface. Col. 7, lines 49-50. Such a semi-rigid or flexible surface material allows the array to adjustably seal against the chamber wells. See, Figures 8a and 8b. Moreover, the '807 patent discloses an apparatus for creating biopolymer arrays on a support surface, wherein the

10/789,678 - 11 -

support may be made of a material that is a "25 μ m thick pliant sheet 56 of polypropylene." Col. 4, lines 60-64.

In view of the proposed Count and these teachings, it would have been obvious to one of ordinary skill in the art to have provided a substrate made from a flexible material in order to adjustably seal against the wells of the plate. Furthermore, the use of a flexible material as a substrate would have been obvious to one of ordinary skill in the art because selection of a known material on the basis of its suitability was a matter of obvious design choice.

Finally, as stated in claim 2, use of mechanical clamps, radiation, heat, external fluid pressure, or adhesives in a microtiter plate were well known in the art. For example, the '334 patent discloses the use of clamps or a frame which joins the chip substrate to a package. Col. 16, line 44 and Figure 20a. Alternatively, screws, clips or adhesives can be used to mate the chip to the package. Col. 16, lines 54-56. Moreover, the '334 patent discloses the use of ultraviolet cured silicone, cement (col. 16, line 34), adhesive films, tape (col. 16, line 40), gaskets or seals (col. 16, line 49), acoustic welding (col. 16, line 52), screws (col. 16, line 54), heat and force (col. 16, line 63-64), insert molding, wave soldering, surface diffusion, laser welding, shrink wrap, o-ring seal, surface etching, or heat staking from the top (col. 17, lines 8-11) as methods used to attach the probe array to the cartridge package. In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used mechanical clamps, radiation, heat, external fluid pressure, or adhesives in the chip package in order to securely mate the chip substrate to a chip package.

Thus, claim 7 would have been obvious over the proposed Count in view of the '334 and '854 or '807 patents and should therefore be designated as corresponding thereto.

10/789,678 - 12 -

Claim 8 is dependent on claim 1 and further recites that the array is made of an optically transparent flexible film having an adhesive surface that surrounds the sets of chemical reactants. Claim 8 further recites that the adhesive surface is contacted with the microtiter plate. Claim 8 would have been obvious over the proposed Count in view of the '334 or '807 patents or U.S. Patent No. 5,856,174 ("the '174 patent"). The '174 patent issued on January 5, 1999 and is a prior art reference against the '702 patent under 35 U.S.C. §102(b).

It was well known in the art that an array could be made of an optically transparent film. For example, the '334 patent teaches that the substrate may be a "flat glass or single-crystal silicon." Col. 4, line 67. The use of these optically transparent elements provides a viewing area into the interior of the reaction cavity. For example, the '174 patent teaches a nucleic acid diagnostic device for performing sample acquisition and preparation operations. The apparatus contains an analytical chamber that is formed with at least one surface having a "transparent window for observation or scanning of the particular analysis being performed." Col. 19, lines 27-29.

Moreover, as stated in claim 7, flexible arrays were well known in the art. The '854 patent discloses an array that is made from a material having a semi-rigid surface. Col. 7, lines 49-50. Such a semi-rigid or flexible surface material allows the array to adjustably seal against the chamber wells. See, Figures 8a and 8b. Additionally, the '807 patent teaches a pliant polypropylene substrate. Col. 4, lines 60-64.

In view of the proposed Count and these teachings, it would have been obvious to one of ordinary skill in the art to have provided an array having a transparent flexible film in order to adjustably seal the array to the plate well and to allow for observation of the interior of the reaction chamber.

10/789,678 - 13 -

Furthermore, the use of adhesives in a microtiter plate was well known in the art. The '334 patent discloses a flow cell device having a ridge (560) that is large enough to receive adhesives for attaching the chip to the package. The adhesive may be an ultraviolet cured silicone, cement, or other adhesive. Col. 16, line 34-35. Thus, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used an adhesive in a microtiter plate in order to attach the chip substrate to the package and provide a tight seal around the flow cell cavity.

Therefore, claim 8 would have been obvious over the proposed Count in view of the '334 and '854 or '807 patents and should therefore be designated as corresponding thereto.

Claim 9 is dependent on claim 1 and further recites that the array is made of a flexible material having an adhesive on a surface that comprises the sets of chemical reactants, and that the adhesive surface is contacted with the microtiter plate. Claim 9 further recites the step of sealing, which includes applying one or more of mechanical clamps, radiation, heat, external fluid pressure, and vacuum to the reaction assembly for a period of time until the adhesive adheres the array to the plate. Claim 9 would have been obvious over the proposed Count in view of the '334 or '854 patents.

As stated in claim 7, an array made of a flexible material was well known in the art. For example, the '334 patent discloses an array made from a flexible material, including materials such as "biological, nonbiological, organic, inorganic, or a combination of any of these, existing as particles, strands, precipitates, gels, sheets, tubing, spheres, containers, capillaries, pads, slices, films, plates, slides, etc." Col. 4, lines 47-51. Furthermore, the '334 patent teaches that the "the wafer may be a polymerized Langmuir Blodgett film, functionalized glass, Si, Ge, GaAs, GaP, SiO₂, SiN₄, modified silicon, or any one of a wide variety of gels or polymers such

10/789,678 - 14 -

as (poly)tetrafluoroethylene, (poly)vinylidenedifluoride, polystyrene, polycarbonate, or combinations thereof." Col. 4, lines 59-64. Many of the materials listed in the '334 patent are flexible. Additionally, the '854 patent discloses an array that is made from a material having a semi-rigid surface. Col. 7, lines 49-50. Such a semi-rigid or flexible surface material allows the array to adjustably seal against the chamber wells. See, Figures 8a and 8b. Moreover, the '807 patent discloses an apparatus for creating biopolymer arrays on a support surface, wherein the support may be made of a material that is a "25 μ m thick pliant sheet 56 of polypropylene." Col. 4, lines 60-64.

In view of the proposed Count and these teachings, it would have been obvious to one of ordinary skill in the art to have provided a substrate made from a flexible material so that the substrate may be able to adjustably seal against the wells of the plate. Furthermore, the use of a flexible material for a substrate would have been obvious to one of ordinary skill in the art because selection of a known material on the basis of its suitability was a matter of obvious design choice.

Moreover, as stated in claim 8 above, the use of adhesives in a microtiter plate was well known. For example, the '334 patent discloses a flow cell device having a ridge (560) that is large enough to receive adhesives for attaching the chip to the package. The adhesive may be an ultraviolet cured silicone, cement, or other adhesive. Col. 16, line 34-35. Thus, it would have been obvious to one of ordinary skill in the art to have used an adhesive in a microtiter plate in order to attach the chip substrate to the package and to provide a tight seal around the flow cell cavity.

Finally, use of mechanical clamps, radiation, heat, external fluid pressure, or adhesives in a microtiter plate were well known in the art. For example, the '334 patent discloses the use of

10/789,678 - 15 -

clamps or a frame which joins the chip substrate to a package. Col. 16, line 44 and Figure 20a. Alternatively, screws, clips or adhesives can be used to mate the chip to the package. Col. 16, lines 54-56. Moreover, the '334 patent discloses the use of ultraviolet cured silicone, cement (col. 16, line 34), adhesive films, tape (col. 16, line 40), gaskets or seals (col. 16, line 49), acoustic welding (col. 16, line 52), screws (col. 16, line 54), heat and force (col. 16, line 63-64), insert molding, wave soldering, surface diffusion, laser welding, shrink wrap, o-ring seal, surface etching, or heat staking from the top (col. 17, lines 8-11), as methods used to attach the probe array to the cartridge package. In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used mechanical clamps, radiation, heat, external fluid pressure, or adhesives in the chip package in order to securely mate the chip substrate to a package.

Thus, claim 9 would have been obvious over the proposed Count in view of the '334 and '854 or '807 patents and should therefore be designated as corresponding thereto.

Claim 10. Claim 10 corresponds to claim 4, except claim 10 depends on claim 9. For essentially the same reasons stated with respect to claim 4, claim 10 should be designated as corresponding to the proposed Count.

Claim 11. Claim 11 is dependent on claim 1 and further recites that the test sample wells are spatially arranged in a surface of the microtiter plate, each well having a side wall adjacent to a closed end that together enclose the well except for an open end at the surface of the microtiter plate, and wherein the ray [sic array] comprises an array substrate having the sets of chemical reactants bound to an ray [sic array] surface of the array substrate in an array pattern of features, the array pattern being similar to the spatial arrangement of test sample wells on the microtiter plate. The proposed Count expressly recites the arrangement of the wells in the

microtiter plate and the pattern of chemical reactants bound to the array surface. Furthermore, the proposed Count states that the open end is opposite the closed end of the well, thus, the open end would inherently be located at the surface of the microtiter plate. Therefore, claim 11 would have been anticipated by the proposed Count and should be designated as corresponding thereto.

Claim 12. Claim 12 is dependent on claim 1 and further recites the step of mechanically agitating a difference in mass densities between the test sample and gas filling any space between the test sample and the set of chemical reactants in each closed cell, which causes mixing of the test sample with the chemical reactants in each closed cell. The '702 patent defines a "gas" as a "substance or mixture of substances, exhibiting zero surface tension and typically having low viscosity." Col. 5, lines 7-8. The '702 patent further defines a "liquid" as "a substance exhibiting surface tension and typically having higher viscosity than a gas." Col. 5, lines 15-17. Moreover, the '702 patent teaches that a fluid can be both a liquid and a gas. Col. 5, lines 20-22.

Claim 12 would have been obvious over the proposed Count in view of the '334 patent. The '334 patent discloses the step of mechanically agitating a chip package using a fluid or liquid test sample and a gas, such a bubble. As disclosed by the '702 disclosure above, liquids and gases exhibit different properties, such as different surface tension, viscosity, and inherently different mass densities. Thus, the bubble disclosed in the '334 patent inherently has a different mass density from the fluid or liquid test sample. Specifically, the '334 patent teaches that the flow device container is filled with a fluid containing targets. Col 7 lines 6-9. Next, bubbles are introduced into the cavity to agitate the test sample. Col. 7, lines 9-10. The agitation of the test sample with the bubble increases the hybridization rate between the targets and complementary probe sequences. Col. 7, lines 12-13.

10/789,678

In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have mechanically agitated a test sample and a gas, such as a bubble, having different mass densities, in order to increase the hybridization rate between target and complementary probe sequences.

Therefore, claim 12 would have been obvious over the proposed Count in view of the '334 patent and should therefore be designated as corresponding thereto.

Claim 13. Claim 13 is dependent on claim 1 and further recites the step of analyzing reaction products in the closed cells after the step of mechanically agitating. Claim 13 would have been obvious over the proposed Count in view of the '334 patent. The '334 patent teaches that after the package is mixed by the vortexer, the package is aligned on a detection or imaging system. Col. 15, lines 45-49. Specifically, the '334 patent teaches that "the imaging systems are capable of qualitatively analyzing the reaction between the probes and targets. Based on this analysis, sequence information of the targets is extracted." Col. 15, lines 53-56. The information is used in various applications, such as in biomedical research, clinical diagnostics, industrial markets, and in emerging field of genomics. Col. 1, lines 51-56.

In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have analyzed the reaction products in order to obtain information on the target sequences for applications in fields including biomedical research or clinical diagnostics.

Therefore, claim 13 would have been obvious over the proposed Count in view of the '334 patent and should therefore be designated as corresponding thereto.

<u>Claim 14</u>. Claim 14 is dependent on claim 13 and further recites that one or both of the microtiter plate and the array is optically transparent. Claim 14 would have been obvious

10/789,678 - 18 -

over the proposed Count in view of the '334, '807 or '174 patents, the Manns *et al.* publication dated May 17-21 1999, entitled "Microplate History 2nd Edition," presented at MipTec-ICAR'99 in Montreux Switzerland or the "New FALCON (R) Cell Culture Inserts Fit 24 Well Plates," news release on April 2, 1991. Both the Manns *et al.* publication and the Falcon news release publication are prior art references against the '702 patent under 35 U.S.C. §102(b). See also, U.S. Patent No. 4,912,035 ('035) which issued March 27, 1990 and is a reference under 35 U.S.C. §102(b). Other patent references that show clear microtiter plates are shown in the attached 1449 form and include U.S. Patent Nos. 5,457,527, 5,319,436, 4,701,754 which are all prior art under 35 U.S.C. §102(b) as well as R. A. Blaheta, et al., Journal of Immunological Methods, 13 Sep 1991, 142(2):199-206.

It was well known in the art that an array or microtiter plate is optically transparent. For example, the '334 patent teaches that the substrate may be a "flat glass or single-crystal silicon." Col. 4, line 67. The use of optically transparent elements provides a viewing area into the interior of the reaction cavity. For example, the '174 patent teaches a nucleic acid diagnostic device for performing sample acquisition and preparation operations. The apparatus contains an analytical chamber that is formed with at least one surface having a "transparent window for observation or scanning of the particular analysis being performed." Col. 19, lines 27-29.

Furthermore, optically transparent microtiter plates were well known in the art. For example, the Manns *et al.* publication describes a microplate or multiwell plate with multiple test tubes. This plate contains a clear or glass bottom. Additionally, the Falcon news release publication describes a 24-well culture plate that is "completely transparent for excellent viewing of the cells." (Page 1, ¶1). Also, '035 shows clear microwell plates were known at col. 6., line

10/789,678 - 19 -

53 where it states "200 μ l of sample was removed, placed in a clear microtiter plate and read at 610 nm.".

Thus, in view of the proposed Count and these teachings, it would have been obvious to one of ordinary skill in the art to have provided an optically transparent array or microtiter plate in order to allow for observation of the interior of the reaction chamber.

Therefore, claim 14 would have been obvious over the proposed Count in view of the '334, '807 '174 patents, the Manns *et al.* publication, or the Falcon news release and should therefore be designated as corresponding thereto.

<u>Claim 15</u>. Claim 15 is dependent on claim 1 and further recites analyzing the reaction products after the step of mechanically agitating, wherein the steps include: disassembling the reaction assembly, rinsing the array and interrogating the array. Claim 15 would have been obvious over the proposed Count in view of the '334 patent.

The '334 patent teaches that the chip array is both rinsed and analyzed. Specifically, the '334 patent states that "the sample is washed with a buffer, which may be 6 X SSPE buffer, to remove the unbound targets. In some embodiments, the cavity is filled with the buffer after washing the sample." Col. 15, lines 41-44. Moreover, the '334 patent teaches that the chips are analyzed using an imaging system that is "capable of qualitatively analyzing the reaction between the probes and targets. Based on this analysis, sequence information of the targets is extracted." Col. 15, lines 54-56. The '334 patent further teaches the assembly of chip package by means including, *inter alia*, sealing two injection molded casings (410 and 420) together. Col. 6, lines 47-52. Thus, the chip package would inherently be capable of disassembly when the seal or other attachment mechanism is removed from the housing.

10/789,678 - 20 -

In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have disassembled, rinsed, and interrogated the array in order to obtain information on the target sequences for application in fields of, *inter alia*, biomedical research or clinical diagnostics.

Thus, claim 15 should be designated as corresponding to the proposed Count.

Claim 16. Claim 16 is dependent on claim 1 and further recites that the microtiter plate is selected from a 96, 234, 384, and 1536 well microtiter plate and that the number of sets of chemical reactants on the array match the selected microtiter plate. Claim 16 would have been obvious over the proposed Count in view of the '334 patent.

The '334 patent teaches a plate having a plurality of cavities, which may be in a 96-well microtiter format. Col. 18, lines 19-20. The '334 patent further discloses that "the probe arrays may be formed on the wafer in a format matching that of the cavities." Col. 18, lines 23-25. This configuration provides significant increased throughput by enabling parallel testing of a plurality of samples. Col. 18, lines 26-28.

In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have provided a 96 well microtiter format in order to enable parallel testing of a plurality of samples. Additionally, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have provided a 234, 384, and 1536 well microtiter plate because the mere duplication or addition of the plate wells involves only routine skill in the art.

Therefore, claim 16 would have been obvious over the proposed Count in view of the '334 patent and should therefore be designated as corresponding thereto.

10/789,678 - 21 -

Claim 17. Claim 17 is dependent on claim 1 and further recites that each set of chemical reactants is an array feature that comprises a subarray having the chemical reactants arranged in a subarray pattern of subfeatures, and wherein the chemical reactant is different in at least one feature or in at least one subfeature on the array. The '702 patent defines features and subarrays as follows:

A feature may include a plurality or a set of 'subfeatures', where each set is a 'subarray'. For the purposes of the invention, there is a plurality of features on an array or microarray, where each feature comprises a plurality of subfeatures. However, the term 'microarray' may be characterized by some skilled in the art as comprising one or more of the subarrays of a larger array. Col. 9, lines 23-30.

Claim 17 would have been obvious over the proposed Count in view of the '334 patent. The '334 patent also discloses such "features" and "subarrays." For example, the '334 patent states that the "substrates have a diverse sequence [of arrays] at known locations on its surface" (Col. 1, line 15) and further teaches that "thousands of different sequences may be fabricated on a single substrate of about 1.28 cm² in only a small fraction of the time required by conventional methods." (Col. 1, lines 47-51). Thus, the '334 patent discloses the use of "subarray" such that thousands of different sequences may be placed on an array.

In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have provided an array having subarrays in order to increase the number of diverse amounts of materials which can be fabricated on a single substrate.

Therefore, claim 17 would have been obvious over the proposed Count in view of the '334 patent and should be designated as corresponding thereto.

Claim 18. Claim 18 is dependent on claim 1 and further recites that the test sample is different in at least one well of the microtiter plate. Claim 18 would have been obvious over the proposed Count in view of the '334 patent.

10/789,678 - 22 -

It was well known in the art that a microtiter plate could contain a plurality of different test samples. For example, the '334 patent teaches a 96-well microtiter format which provides significant increased throughput by enabling parallel testing of a plurality of samples. Col. 18, lines 18-28. Thus, in view of the '334 patent, it would have been obvious to one of ordinary skill in the art to have provided a microtiter plate having a test sample that is different in at least one well in order to enable parallel testing of different samples.

Therefore, claim 18 should be designated as corresponding to the proposed Count.

Claim 19 is an independent claim which recites a method of Claim 19. simultaneously conducting multiple chemical reactions between a first chemical sample and a second chemical sample comprising the steps of providing a plate having a plurality of wells spatially arranged in a surface of the plate in a well array pattern, each well having a side wall adjacent to a closed end that enclose the well except for an open end that is opposite the closed end and that is adjacent to the plate surface. The plurality of wells in the plate receive the first chemical sample via the open end of the well. Claim 19 further recites the method of providing an array of the second chemical sample, the ray [sic array] comprising sets of the second chemical sample bound to and spatially arranged on a surface of an array substrate in an array pattern of features, the well array pattern being spatially similar to the feature array pattern. Additionally, claim 19 recites assembling the array onto the plate to form a sealed reaction assembly, such that the surface of the array faces the surface of the plate and encloses the open ends of the plurality of wells to form closed cells, each closed cell comprising the first chemical sample and a respective set of the second chemical sample features, wherein the sealed reaction assembly is one or more of gas tight, liquid tight, and fluid tight. Finally, claim 19 recites the method of contacting the first chemical sample with the second chemical sample in each closed

10/789,678 - 23 -

cell of the sealed reaction assembly. Claim 19 would have been obvious over the proposed Count in view of the '334 patent.

Assembling an array plate as claimed was well known in the art. For example, the '334 patent teaches a 96-well microtiter plate having a chip mounted individually to each cavity. Col. 18, lines 21-23. Alternatively, the '334 patent teaches that the probe arrays may be formed on the wafer in a format matching that of the cavities. Col. 18, lines 23-25. Moreover, the '334 patent discloses several fluid retaining seals, such as gaskets, which are used in the assembly of the chip package. Col. 16, line 49. The gasket or seal (2070) is located between the ledge and chip to ensure a tight seal around cavity (310). Col. 16, lines 49-50. Thus, it would have been obvious to one of ordinary skill in the art to have provided the assembly as recited in claim 19 in order to effectively match the wells with the substrate arrays for hybridization and to provide a tight seal around the reaction cavity.

Furthermore, the step of contacting a first chemical sample with a second chemical sample was well known in the art. For example, the '334 patent discloses a vortexer which mixes and contacts the test sample contents with the probe arrays. The chip package of the '334 patent is mounted on a vortexer (2910) to vibrate the chip package. Col. 19, line 43-44. The vortexer mixes targets in the fluid with the probe arrays located on the chip, increasing the hybridization rate between the targets and complementary probe sequences. Col. 19, lines 40-50 and col. 7, lines 11-12.

Thus, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to create an embodiment of claim 19, in which the chemical samples are contacted in the wells of the microtiter plate in order to mix the sample and increase hybridization between the target and complementary probe sequences.

10/789,678 - 24 -

Therefore, claim 19 should be designated as corresponding to the proposed Count.

Claim 20. Claim 20 corresponds substantially to claim 7, except that claim 20 depends from claim 19. For essentially the same reasons as stated in claim 7 above, claim 20 should be designated as corresponding to the proposed Count.

Claim 21. Claim 21 depends from claim 20 and further recites that the array substrate is made of an optically transparent flexible film having an adhesive on the surface to which the second chemical samples are bound, the adhesive surrounding the features, and in the step of assembling, the adhesive is contacted with the plate surface to seal the reaction assembly. Claim 21 would have been obvious over the proposed Count in view of the '334 patent and the '807, '174 or '854 patents.

It was well known in the art that an array could be made of an optically transparent film. For example, the '334 patent teaches that the substrate may be a "flat glass or single-crystal silicon." Col. 4, line 67. The use of optically transparent elements provides a viewing area into the interior of the reaction cavity. For example, the '174 patent teaches a nucleic acid diagnostic device for performing sample acquisition and preparation operations. The apparatus contains an analytical chamber that is formed with at least one surface having a "transparent window for observation or scanning of the particular analysis being performed." Col. 19, lines 27-29.

Additionally, flexible films were well known in the art. For example, the '334 patent discloses several materials that may be used in the construction of the substrate wafer, including, among others, "biological, nonbiological, organic, inorganic, or a combination of any of these, existing as particles, strands, precipitates, gels, sheets, tubing, spheres, containers, capillaries, pads, slices, films, plates, slides, etc." Col. 4, lines 47-51. Furthermore, the '334 patent teaches that "the wafer may be a polymerized Langmuir Blodgett film, functionalized glass, Si, Ge,

10/789,678 - 25 -

GaAs, GaP, SiO₂, SiN₄, modified silicon, or any one of a wide variety of gels or polymers such as (poly)tetrafluoroethylene, (poly)vinylidenedifluoride, polystyrene, polycarbonate, or combinations thereof." Col. 4, lines 59-64. Many of the materials listed in the '334 patent are flexible. Additionally, the '854 patent discloses an array that is made from a material having a semi-rigid surface. Col. 7, lines 49-50. Such a semi-rigid or flexible surface material allows the array to adjustably seal against the chamber wells. See, Figures 8a and 8b. Moreover, the '807 patent discloses a support surface used in an apparatus for creating biopolymer arrays, wherein the support may be a pliant substrate. Col. 4, lines 60-64.

In view of the proposed Count and these teachings, it would have been obvious to one of ordinary skill in the art to have provided an array having a transparent flexible film in order to adjustably seal the array to the plate well and to allow for observation of the interior of the reaction chamber.

Furthermore, the use of adhesives in a microtiter plate was well known in the art. The '334 patent discloses a flow cell device having a ridge (560) that is large enough to receive adhesives for attaching the chip to the package. The adhesive may be an ultraviolet cured silicone, cement, or other adhesive. Col. 16, line 34-35. Thus, it would have been obvious to one of ordinary skill in the art to have used an adhesive on the substrate, which would inherently surround the features in order to securely attach the chip substrate to the package and provide a tight seal around the cavity.

Therefore, claim 21 would have been obvious over the proposed Count in view of the '334 patent and the '807, '174 or '854 patents and should therefore be designated as corresponding thereto.

Claim 22. Claim 22 corresponds substantially to claim 9, except that claim 22 depends from claim 20. For essentially the same reasons as stated in claim 9 above, claim 22 should be designated as corresponding to the proposed Count.

Claim 23. Claim 23 corresponds substantially to claim 10, except that claim 23 depends from claim 22. For essentially the same reasons as stated in claim 10 above, claim 23 should be designated as corresponding to the proposed Count.

Claim 24. Claim 24 corresponds substantially to claim 2, except that claim 24 depends from claim 19. For essentially the same reasons as stated in claim 2 above, claim 24 should be designated as corresponding to the proposed Count.

<u>Claim 25</u>. Claim 25 corresponds substantially to claim 5, except that claim 25 depends from claim 24. For essentially the same reasons as stated in claim 5 above, claim 25 should be designated as corresponding to the proposed Count.

Claim 26. Claim 26 depends from claim 19 and further recites the step of providing a gasket having a plurality of through holes spatially ranged [sic arranged] through a thickness of the gasket in a through hole array pattern, wherein the well pattern, the array pattern and the through hole pattern are dimensionally and spatially similar, and the gasket being made of a pliable material. The step of assembling comprises placing the pliable gasket between the plate surface and the array surface, such that the plurality of through holes are aligned with the features of the second chemical sample and the wells, and sealing the gasket to the array and the plate using one or more of mechanical clamps, radiation, heat, external fluid pressure, vacuum and an adhesive to seal the reaction assembly. Claim 26 would have been obvious over the proposed Count in view of the '334 patent.

10/789,678 - 27 -

The proposed Count recites, *inter alia*, a seal between the plate and the array that is one or more of gas tight, liquid tight, and fluid tight. It was well known in the art to use a gasket having through holes. For example, the '334 patent discloses several fluid retaining seals, including gaskets or seals. Col. 16, line 49. The gasket or seal (2070) is located between the ledge of the chip apparatus and the chip substrate to ensure a tight seal around cavity (310). Col. 16, lines 49-50. This gasket, when used in a microtiter body, would inherently contain through holes to allow mixing of the probe and target sequences. (See description of microtiter body at col. 18, lines 18-28). Thus, it would have been obvious to the skilled artisan to create an embodiment of claim 26, in which the seal of the microtiter plate is a gasket with through holes that align with the test samples in order to ensure a tight seal around a cavity, while concurrently allowing the test sample to effectively mix and hybridize with the probe array.

Assembling an array plate as claimed was well known in the art. For example, the '334 patent teaches a 96-well microtiter plate having a chip mounted individually to each cavity. Col. 18, lines 21-23. Alternatively, the '334 patent teaches that the probe arrays may be formed on the wafer in a format matching that of the cavities. Col. 18, lines 23-25. Additionally, as described above, the '334 patent discloses a gasket, which is used in the assembly of the chip package. Col. 16, line 49. The gasket or seal (2070) is located between the ledge and the chip to ensure a tight seal around cavity (310). Col. 16, lines 49-50. Thus, it would have been obvious to one of ordinary skill in the art to have provided for the assembly as recited in claim 26 in order to effectively match the wells with the substrate arrays for hybridization and to provide for a tight seal around the reaction cavity.

Furthermore, use of mechanical clamps, radiation, heat, external fluid pressure, or adhesives in a microtiter plate were well known in the art. For example, the '334 patent

10/789,678 - 28 -

discloses the use of clamps or a frame which attaches the chip substrate to a package. Col. 16, line 44 and Figure 20a. Alternatively, screws, clips or adhesives which can be used to mate the chip to the package. Col. 16, lines 54-56. Moreover, the '334 patent discloses the use of ultraviolet cured silicone, cement (col. 16, line 34), adhesive films, tape (col. 16, line 40), gaskets or seals (col. 16, line 49), acoustic welding (col. 16, line 52), screws (col. 16, line 54), heat and force (col. 16, line 63-64), insert molding, wave soldering, surface diffusion, laser welding, shrink wrap, o-ring seal, surface etching, or heat staking from the top (col. 17, lines 8-11), as methods used to attach the probe array to the cartridge package. In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used mechanical clamps, radiation, heat, external fluid pressure, or adhesives in the chip package to securely mate the substrate to a chip package.

Thus, claim 26 would have been obvious over the proposed Count in view of the '334 patent and should therefore be designated as corresponding thereto.

Claim 27. Claim 27 depends from claim 26 and further recites that the pliable gasket comprises the adhesive on at least one surface adjacent either the plate surface or the array surface. Claim 27 would have been obvious over the proposed Count in view of the '334 patent.

The '334 patent discloses a flow cell device having a gasket or seal (2070) which is located between the ledge of the flow cell device and the chip substrate to ensure a tight seal around the cavity (310). Col. 16, lines 49-50. The device further includes a ridge (560) that is large enough to receive adhesives for attaching the chip to the package. The adhesive may be an ultraviolet cured silicone, cement, or other adhesive. Col. 16, line 34-35. Because the gasket is located next to the chip, the gasket would inherently contain the adhesives on at least one surface in order to attach the chip substrate to the package. Thus, it would have been obvious to one of

10/789,678 - 29 -

ordinary skill in the art to have provided an adhesive on the surface of a gasket in order to attach the chip to the package and thus provide a tight seal around the cavity.

Therefore, claim 27 should be designated as corresponding to the proposed Count.

Claim 28. Claim 28 corresponds substantially to claim 4, except claim 28 depends from claim 27. For essentially the same reasons as claim 4 above, claim 28 should be designated as corresponding to the proposed Count.

Claim 29. Claim 29 corresponds substantially to claim 5, except that claim 29 depends from claim 26. For essentially the same reasons as stated in claim 5 above, claim 29 should be designated as corresponding to the proposed Count.

Claim 30. Claim 30 depends from 19 and further recites the step of contacting, including one or more of mechanically agitating the reaction assembly, controlling the reaction temperature of the reaction assembly, directing radiation into the assembly, and inverting the reaction assembly to cause mixing between the first chemical sample and the second chemical sample. Claim 30 would have been obvious over the proposed Count in view of the '334 or '174 patents.

Temperature control in a flow cell container was well known in the art. For example, the '334 patent discloses that an opening is formed in the flow cell below the cavity "to receive a temperature controller for controlling the temperature in the cavity. By forming a sealed thermostatically controlled chamber in which fluids can easily be introduced, a practical medium for sequencing by hybridization is provided." Col. 2, lines 1-7. Additionally, the '174 patent teaches an amplification chamber having a temperature controller for heating the reaction to carry out thermal cycling. Col. 18, lines 53-55. The temperature controlled reaction chamber allows for rapid heating and cooling of reagents. Col. 18, lines 64-65. Thus, in view of the

10/789,678 - 30 -

proposed Count and the '334 or '174 patents, it would have been obvious to one of ordinary skill in the art to have controlled the temperature of the reaction assembly in order to allow for rapid heating and cooling of reagents.

Additionally, the step of directing radiation into a flow cell was well known in the art. The '334 patent discloses that ultrasonic radiation may be employed to force a buffer to flow through the flow cell device. Col. 20, lines 56-63. Thus, it would have been obvious to one of ordinary skill in the art to have directed radiation into the flow cell in order to force fluid flow.

Finally, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have inverted the reaction assembly. As stated previously in claim 1, the '334 patent discloses a vortexer which mixes targets in the fluid with the probe arrays located on the chip, increasing the hybridization rate between the targets and complementary probe sequences. Col. 19, lines 40-50 and col. 7, lines 11-12. The vortexer rotates, thus inverting, the chip package until hybridization is completed. Col. 19, lines 46-49. Thus, in view of the proposed Count and the teachings of the '334 patent, it would have been obvious to one of ordinary skill in the art to have inverted a chip package in order to increase the hybridization between target and probe sequences.

Therefore, claim 30 should be designated as corresponding to the proposed Count.

Claim 31. Claim 31 depends on claim 19 and further recites the steps of providing a gasket having a plurality of spatially arranged through holes, the arrangement of through holes being similar to the arrangement of the wells and of the array pattern, the gasket being made of a pliable material. Further, claim 31 recites introducing an aliquot of the first chemical sample into each well of the plate, the first chemical sample being fluid and partially filling the wells, and introducing a volume of a second fluid to the wells, the second fluid having a mass density

10/789,678 - 31 -

that is different from a mass density of the first chemical sample and the second fluid being nonreactive with the first chemical sample and second chemical sample. These steps recited in claim
31 occur before the step of assembling. The following steps recited in claim 31 occur during
assembling, including placing the gasket on the surface of the plate, placing the array on the
gasket, such that the array features are aligned with the through holes and the wells, and sealing
the plate, the gasket and the array together using one or more of mechanical clamps, radiation,
heat, external fluid pressure, vacuum and an adhesive, and wherein the step of contacting
comprises mechanically agitating the reaction assembly to mix the first chemical sample and the
second chemical sample in each closed reaction cell.

Claim 31 would have been obvious over the proposed Count in view of the '334 patent. The proposed Count recites, *inter alia*, a seal between the plate and the array that is one or more of gas tight, liquid tight, and fluid tight. It was well known in the art to use a seal or gasket having through holes. For example, the '334 patent discloses several fluid retaining seals, including gaskets or seals. Col. 16, line 49. The gasket or seal (2070) is located between the ledge of the chip apparatus and the chip substrate to ensure a tight seal around cavity (310). Col. 16, lines 49-50. This gasket, when used in a microtiter body, would have inherently contained through holes to allow mixing of the probe and target sequences. (See description of microtiter body at col. 18, lines 18-28). Thus, it would have been obvious to the skilled artisan to create an embodiment of claim 31, in which the seal of the microtiter plate is a gasket with through holes that align with the test samples in order to ensure a tight seal around a cavity, while concurrently allowing the test sample to effectively mix and hybridize with the probe array.

Furthermore, the '334 patent discloses the step of mechanically agitating a chip package using a test sample and a gas, such as a bubble. The bubble disclosed in the '334 patent

10/789.678 - 32 -

inherently has a different mass density from the liquid test sample. The '702 patent defines a "gas" as a "substance or mixture of substances, exhibiting zero surface tension and typically having low viscosity." Col. 5, lines 7-8. The '702 patent further defines a liquid as a substance "exhibiting surface tension and typically having higher viscosity than a gas." Col. 5, lines 15-17. Moreover, the '702 patent teaches that a fluid can be both a liquid and a gas. Col. 5, lines 20-22.

The '334 patent discloses the step of mechanically agitating a chip package using a test sample and a gas, such a bubble. As disclosed by the '702 disclosure above, liquids and gases exhibit different properties, such as different surface tension, viscosity, and inherently different densities. Thus, the gas bubble of the '334 patent would inherently have a different mass density from the fluid or liquid test sample. Specifically, the '334 patent teaches that the flow device container is filled with a fluid containing targets. Col 7 lines 6-9. Next, bubbles are introduced into the cavity to agitate the test sample. Col. 7, lines 9-10. The agitation of the test sample with the bubble increases the hybridization rate between the targets and complementary probe sequences. Col. 7, lines 12-13. Thus, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have mechanically agitated a test sample and a gas, such as a bubble, having different mass densities, in order to increase the hybridization rate between target and complementary probe sequences.

Moreover, use of mechanical clamps, radiation, heat, external fluid pressure, or adhesives in a microtiter plate were well known in the art. For example, the '334 patent discloses the use of clamps or a frame which joins the chip substrate to a package. Col. 16, line 44 and Figure 20a. Alternatively, screws, clips or adhesives can be used to mate the chip to the package. Col. 16, lines 54-56. Moreover, the '334 patent discloses the use of ultraviolet cured silicone, cement (col. 16, line 34), adhesive films, tape (col. 16, line 40), gaskets or seals (col. 16, line 49),

10/789,678 - 33 -

acoustic welding (col. 16, line 52), screws (col. 16, line 54), heat and force (col. 16, line 63-64), insert molding, wave soldering, surface diffusion, laser welding, shrink wrap, o-ring seal, surface etching, or heat staking from the top (col. 17, lines 8-11), as methods used to attach the probe array to the cartridge package. In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used mechanical clamps, radiation, heat, external fluid pressure, or adhesives in the chip package in order to secure the chip substrate to a chip package.

Finally, the '334 patent teaches the steps of assembly, as recited in claim 31. A section titled Parallel Hybridization and Diagnostics in the '334 patent discloses:

In an alternative embodiment, the body is configured with a plurality of cavities. The cavities, for example, may be in a 96-well micro-titre format. In some embodiments, a chip is mounted individually to each cavity according to the methods described above. Alternatively, the probe arrays may be formed on the wafer in a format matching that of the cavities. Accordingly, separating the wafer is not necessary before attaching the probe arrays to the package. This format provides significant increased throughput by enabling parallel testing of a plurality of samples. Col. 18, lines 18-28.

Thus, in view of the proposed Count and the '334 patent, the steps of assembly recited in claim 31 would have been obvious to one of ordinary skill in the art because assembly of working parts recited in a prior art references involves only routine skill in the art.

Therefore, claim 31 should be designated as corresponding to the proposed Count.

Claim 32. Claim 32 corresponds substantially to claim 12, except that claim 32 depends on claim 31. For essentially the same reasons as stated in claim 12 above, claim 32 should be designated as corresponding to the proposed Count.

<u>Claim 33</u>. Claim 33 corresponds substantially to claim 5, except that claim 33 depends on claim 31. For essentially the same reasons as stated in claim 5 above, claim 33 should be designated as corresponding to the proposed Count.

<u>Claim 34</u>. Claim 34 corresponds substantially to claim 6, except that claim 34 depends on claim 33. For essentially the same reasons as stated in claim 6 above, claim 34 should be designated as corresponding to the proposed Count.

Claim 35. Claim 35 corresponds substantially to claim 3, except that claim 35 depends on claim 31. For essentially the same reasons as stated in claim 3 above, claim 35 should be designated as corresponding to the proposed Count.

Claim 36. Claim 36 depends on claim 35 and further recites that the gasket is made of a flexible adhesive film. Claim 36 would have been obvious over the proposed Count in view of the proposed Count and the '334 patent. The '334 patent teaches several types of seals, including gaskets and tapes. As shown in Figure 24, the seal is a tape which comprises a non-permanent adhesive used to ensure a tight seal around the cavity. Col. 17, lines 26-29. Thus, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have provided a gasket made of a flexible adhesive film in order to ensure a tight seal around the cavity. Furthermore, the material selection of the gasket was a matter of obvious design choice within the skilled in the art.

<u>Claim 37</u>. Claim 37 is specifically recited in the proposed Count. Therefore, claim 37 would have been anticipated by the proposed Count and should be designated as corresponding thereto.

<u>Claim 38</u>. Claim 38 is dependent on claim 37 and substantially recites a combination of limitations that are shown in claims 2 and 3. For essentially the same reasons as stated in claims 2 and 3, claim 38 should be designated as corresponding to the proposed Count.

Claim 39. Claim 39 corresponds substantially to claim 36, except that claim 39 depends on claim 38. For essentially the same reasons as stated in claim 36 above, claim 39 should be designated as corresponding to the proposed Count.

<u>Claim 40</u>. Claim 40 corresponds substantially to claim 5, except that claim 40 depends on claim 38. For essentially the same reasons as stated in claim 5 above, claim 40 should be designated as corresponding to the proposed Count.

Claim 41. Claim 41 depends from claim 38 and further recites that the pliable gasket is integral with the surface of the plate. Claim 41 would have been obvious over the proposed Count in view of the '334 patent.

The proposed Count recites, *inter alia*, a seal between the plate and the array that is one or more of gas tight, liquid tight, and fluid tight. It was well known in the art to use a seal or gasket to seal fluids in a microtiter plate. For example, the '334 patent discloses several fluid retaining seals, including gaskets or seals. Col. 16, line 49. The gasket or seal (2070) is located between the ledge of the chip apparatus and the chip substrate to ensure a tight seal around the cavity (310). Col. 16, lines 49-50.

Thus, it would have been obvious to one of ordinary skill in the art to have provided for an integral gasket to seal the reaction chamber because forming a gasket and the plate in one piece which has formerly been formed in two pieces involves only routine skill in the art.

Therefore, claim 41 would have been obvious over the proposed Count in view of the '334 patent and should be designated as corresponding thereto.

<u>Claim 42</u>. Claim 42 depends on claim 37 and further recites that the seal comprises the array substrate being made of a flexible material and one or more of mechanical clamps,

radiation, heat, external fluid pressure, vacuum and an adhesive. Claim 42 would have been obvious over the proposed Count in view of the '334 patent and the '854 or '807 patents.

Flexible array substrates were well known in the art. The '334 patent discloses an array made from a flexible material. For example, the '334 patent discloses several materials that may be used in the construction of the substrate wafer, including, among others, "biological, nonbiological, organic, inorganic, or a combination of any of these, existing as particles, strands, precipitates, gels, sheets, tubing, spheres, containers, capillaries, pads, slices, films, plates, slides, etc." Col. 4, lines 47-51. Furthermore, the '334 patent teaches that the "the wafer may be a polymerized Langmuir Blodgett film, functionalized glass, Si, Ge, GaAs, GaP, SiO₂, SiN₄, modified silicon, or any one of a wide variety of gels or polymers such as polycarbonate, (poly)tetrafluoroethylene, (poly)vinylidenedifluoride, polystyrene, or combinations thereof." Col. 4, lines 59-64. Many of the materials listed in the '334 patent are flexible. Additionally, the '854 patent discloses an array that is made from a material having a semi-rigid surface. Col. 7, lines 49-50. Such a semi-rigid or flexible surface material allows the array to adjustably seal against the chamber wells. See, Figures 8a and 8b. Moreover, the '807 patent discloses a support surface used in an apparatus for creating biopolymer arrays, wherein the support may be a pliant substrate. Col. 4, lines 60-64.

In view of the proposed Count and these teachings, it would have been obvious to one of ordinary skill in the art to have provided a substrate made from a flexible material in order to adjustably seal against the wells of the plate. Furthermore, the use of a flexible material for a substrate would have been obvious to one of ordinary skill in the art because selection of a known material on the basis of its suitability was a matter of obvious design choice.

10/789,678 - 37 -

Furthermore, use of mechanical clamps, radiation, heat, external fluid pressure, or adhesives in a microtiter plate were well known in the art. For example, the '334 patent discloses the use of clamps or a frame which joins the chip substrate to a package. Col. 16, line 44 and Figure 20a. Alternatively, screws, clips or adhesives can be used to mate the chip to the package. Col. 16, lines 54-56. Moreover, the '334 patent discloses the use of ultraviolet cured silicone, cement (col. 16, line 34), adhesive films, tape (col. 16, line 40), gaskets or seals (col. 16, line 49), acoustic welding (col. 16, line 52), screws (col. 16, line 54), heat and force (col. 16, line 63-64), insert molding, wave soldering, surface diffusion, laser welding, shrink wrap, o-ring seal, surface etching, or heat staking from the top (col. 17, lines 8-11), as methods used to attach the probe array to the cartridge package. In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used mechanical clamps, radiation, heat, external fluid pressure, or adhesives in the chip package in order to mate the chip substrate to a chip package.

Therefore, claim 42 would have been obvious over the proposed Count in view of the '334 patent and the '854 or '807 patents and should be designated as corresponding thereto.

Claim 43. Claim 43 corresponds substantially to claim 8, except that claim 43 depends on claim 37. For essentially the same reasons as stated in claim 8 above, claim 43 should be designated as corresponding to the proposed Count.

<u>Claim 44</u>. Claim 44 corresponds substantially to claim 23, except that claim 44 depends on claim 37. For essentially the same reasons as stated in claim 23 above, claim 44 should be designated as corresponding to the proposed Count.

<u>Claim 45</u>. Claim 45 depends on claim 44 and further recites that the releasable adhesive is an ultraviolet light-releasable adhesive.

10/789,678 - 38 -

Releasable and ultraviolet light adhesives were well known in the art. For example, the '334 patent discloses a tape that is comprised of non-permanent adhesive. Col. 17, lines 26-27. The non-permanent adhesive is placed over the inlets of the flow device to be sealed or unsealed without completely separating the tape from the package. Col. 17, lines 26-27. Thus, the removable adhesive allows for convenient sealing and resealing of the flow cell without completely removing the tape.

Additionally, the '334 patent discloses ultraviolet adhesives. The '334 patent teaches a flow cell device having a ridge (560) that is large enough to receive adhesives for attaching the chip substrate to the package. The adhesive may be an ultraviolet cured silicone. Col. 16, line 34-35.

Thus, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have provided an adhesive as recited in claim 45, in order to allow convenient sealing and resealing of the flow cell device.

Therefore, claim 45 should be designated as corresponding to the proposed Count.

Claim 46. Claim 46 corresponds substantially to claim 16, except that claim 46 depends on claim 41. For essentially the same reasons as stated in claim 16 above, claim 46 should be designated as corresponding to the proposed Count.

Claim 47. Claim 47 is specifically recited in the proposed Count. Therefore, claim 47 would have been anticipated by the proposed Count and should be designated as corresponding thereto.

Claim 48. Claim 48 depends on claim 47 and further recites one or more of a pliable gasket having a plurality of spatially arranged through holes similar to the spatial arrangement of the wells and the sets of reactants, the pliable gasket providing the seal between the plate and the

10/789,678 - 39 -

array when combined wit [sic with] one or more of mechanical clamps, radiation, heat, external fluid pressure, vacuum and an adhesive, an adhesive for sealing at least the array and the plate, a sample biological material for a control experiment, instructions for simultaneously conducting multiple reactions, and instructions for assembling the array to the plate. Claim 48 would have been obvious over the proposed Count in view of the '334 patent.

The proposed Count recites, *inter alia*, a seal between the plate and the array that is one or more of gas tight, liquid tight, and fluid tight. It was well known in the art to use a gasket having through holes. For example, the '334 patent discloses several fluid retaining seals, including gaskets or seals. Col. 16, line 49. The gasket or seal (2070) is located between the ledge of the chip device and the chip substrate to ensure a tight seal around cavity (310). Col. 16, lines 49-50. This gasket, when used in the microtiter body, would inherently contain through holes to allow mixing of the probe and target sequences. (See description of microtiter body at col. 18, lines 18-28). Thus, it would have been obvious to the skilled artisan to create an embodiment of claim 48, in which the seal of the microtiter plate is a gasket with through holes that align with the test samples in order to ensure a tight seal around a cavity, while concurrently allowing the test sample to effectively mix and hybridize with the probe array.

Furthermore, use of mechanical clamps, radiation, heat, external fluid pressure, or adhesives in a microtiter plate were well known in the art. For example, the '334 patent discloses the use of clamps or a frame which joins the chip substrate to a package. Col. 16, line 44 and Figure 20a. Alternatively, screws, clips or adhesives can be used to mate the chip to the package. Col. 16, lines 54-56. Moreover, the '334 patent discloses the use of ultraviolet cured silicone, cement (col. 16, line 34), adhesive films, tape (col. 16, line 40), gaskets or seals (col. 16, line 49), acoustic welding (col. 16, line 52), screws (col. 16, line 54), heat and force (col. 16,

10/789,678 - 40 -

line 63-64), insert molding, wave soldering, surface diffusion, laser welding, shrink wrap, o-ring seal, surface etching, or heat staking from the top (col. 17, lines 8-11), as methods used to attach the probe array to the cartridge package. In view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used mechanical clamps, radiation, heat, external fluid pressure, or adhesives in the chip package in order to securely mate the substrate to a chip package.

Additionally, the use of adhesives in flow cells were well known in the art. For example, the '334 patent discloses a tape that is comprised of non-permanent adhesive and ultraviolet adhesives. Col. 17, lines 26-27. The adhesive allows for convenient sealing and resealing and ensures a tight seal around the cavity of the flow cell. Thus, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have provided an adhesive as recited in claim 48, in order to allow for a tight seal around the cavity.

Moreover, the use of biological sample, for testing the array was well known in the art. The '334 patent defines a target as a molecule that has an affinity for a given probe and is sometimes referred to as a receptor. Col. 4, lines 12-13. Examples of targets include antibodies, cell membrane receptors, nucleic acids, and other biological samples. Col. 4, lines 21-27. Thus, in view of the proposed Count and the '334 patent, it would have been obvious to one of ordinary skill in the art to have used a biological sample for the testing of an array in order to provide complementary binding with the probe arrays.

Finally, instructions for simultaneously conducting multiple reactions and instructions for assembling the array to the plate were well known in the art. The '334 patent provides disclosure which instructs one of ordinary skill in the art to conduct reactions and assemble the probe array. For example, col. 15, lines 25 to 36 provides instructions for conducting reactions ("usually,

10/789,678 - 41 -

hybridization is performed by first exposing the sample with a prehybridization solution. Next, the sample is incubated under binding conditions with a solution containing targets for a suitable binding period....") and col. 18, lines 18-28 further provides instructions for assembling a microtiter plate ("a chip is mounted individually to each cavity according to the methods described above. Alternatively, the probe arrays may be formed on the wafer in a format matching that of the cavities. Accordingly, separating the wafer is not necessary before attaching the probe arrays to the package..."). Thus, it would have been obvious to one of ordinary skill in the art to have provided instructions for assembling and conducting reactions in a flow cell in order to teach users how to properly conduct assays.

Claim 49. Claim 49 is an independent claim which recites a method of simultaneously conducting multiple chemical reactions in a reaction assembly that includes a microtiter plate of wells containing test samples and an array of sets of chemical reactants. The steps recited in claim 49 include: assembling the array of sets of chemical reactants to the microtiter plate of test samples such that the may [sic array] covers open ends in the test sample wells of the microtiter plate to form a plurality of closed cells, each closed cell comprising a set of chemical reactants and a respective test sample, the sets of chemical reactants being bound to an array surface of the array, sealing the microtiter plate to the array to create one or more of a gas tight, a liquid tight, and a fluid tight seal, and mechanically agitating the sealed reaction assembly to contact the test samples with the array-bound chemical reactants in each closed cell simultaneously. Claim 49 would have been obvious over the proposed Count in view of the '334 patent.

Claim 49 is substantially similar to claim 1 with the addition of the chemical reactants being bound to the surface of the array. However, the proposed Count expressly recites that a

10/789,678 - 42 -

plurality of sets of chemical reactants are spatially arranged on an array substrate. Thus, for essentially the same reasons as claim 1, claim 49 should be designated as corresponding to the proposed Count.

2. Designation of Applicants' Claims 141-163

Applicants identify Applicants' claims 141-158 and 160-162 as corresponding to the proposed Count. Applicants' claims 159 and 163 are expressly recited in the definition of the proposed Count and, therefore, would have been anticipated by the proposed Count. Applicants' claims 141, 143, 146-148, 151-153, 155-156, 158-159, 161, and 163 correspond exactly to the '702 patent claims 1, 8, 11-13, 17-19, 21-22, 30, 37, 43, and 47, respectively, and should be designated as corresponding to the proposed Count. Applicants' claims 142, 144-145, 149-150, 154, 157, 160, and 162 are substantially similar to the '702 patent claims 7, 9-10, 14, 16, 20, 23, 42, and 44, respectively, and should be designated as corresponding to the proposed Count. Accordingly, Applicants' claims 141-158 and 160-162 should be designated as corresponding to the proposed Count.

IV. 37 C.F.R. §§ 41.202 (a)(4) and 41.202(d) - Applicants will prevail on priority

Applicants' present application claims benefit through a series of continuation applications to an application filed on Junc 7, 1995, *i.e.*, U.S. Patent Application No. 08/485,452 ("the '452 application") and the '452 application claims priority as a continuation in part to an application filed June 8, 1994, U.S. Serial No. 08/255,682 ("the '682 application"). The chart set forth in Appendix C shows that the '682 application provides a constructive reduction to practice an embodiment within the scope of the interfering subject matter. In comparison, the earliest possible constructive reduction to practice to which the '702 patent may be accorded benefit is U.S. Patent Application No. 09/938,909, filed on August 24, 2001.

10/789,678 - 43 -

Therefore, Applicants will *prima facie* prevail on priority based on a constructive reduction to practice that precedes by <u>seven years and two months</u> the earliest <u>possible</u> constructive reduction to practice that <u>may</u> be accorded to the '702 patent.

V. 37 C.F.R. §§ 41.202(a)(5) - Written Description for each claim in the Applicants' Specification

Applicants notify the Examiner that there is written description support in the '678 application for newly added claims 141-163.

Specifically, on page 27, lines 11-17, Applicants' specification discloses a parallel hybridization diagnostics. The '678 application describes a body that is configured with a plurality of cavities, which may be a 96-well microtiter format. Probe arrays are formed on the surface of the chip wafer in a format matching those of the cavities. The parallel hybridization package enables increased throughput because multiple wells are tested with a plurality of samples. Similarly, the '702 patent describes a method and apparatus for conducting multiple chemical reactions. During prosecution of the 09/938,909 application (now the '702 patent), Barth *et al.* stated that the "invention comprises both a microtiter plate of wells containing test samples and array of sets of chemical reactants that are assembled together to form a reaction assembly for simultaneously conduct multiple chemical reactions." (See, Appendix E - Response to Official Action, dated 06/19/03, page 14). Thus, the subject matter of the '678 application and the '702 patent are substantially similar and written description support is shown throughout the '678 application for claims 141-163.

Applicants have added claims 141-163 to provoke the suggested interference. In accordance with 37 C.F.R. § 41.202(a)(5), Applicants provide a claim chart in Appendix B showing the written description in the Applicants' specification for newly added claims 141-163.

10/789,678 - 44 -

VI. 37 C.F.R. § 41.202(a)(6) – Applicants' Earliest Constructive Reduction to Practice

For the purpose of the suggested interference, Applicants are entitled to the benefit of the '682 application, filed June 8, 1994, which constitutes a constructive reduction to practice of an embodiment within the scope of the interfering subject matter, as reflected in Appendix C. According to 37 C.F.R. § 41.201, a "constructive reduction to practice" means "a described and enabled anticipation under 35 U.S.C. 102(g)(1) in a patent application of the subject matter of a count." Likewise, pursuant to 37 C.F.R. § 41.201, an "earliest constructive reduction to practice" means "the first constructive reduction to practice that has been continuously disclosed through a chain of patent applications including in the involved application or patent. For the chain to be continuous, each subsequent application must have been co-pending under 35 U.S.C. 120 or 121 or timely filed under 35 U.S.C. 119 or 365(a)."

A constructive reduction to practice of an embodiment within the scope of the interfering subject matter has been continuously disclosed from the earliest filed application, 08/255,682, filed June 8, 1994, to a continuation-in-part application 08/485,452, filed June 7, 1995, through a series of continuation applications, to the present application. Specifically, the present application is a continuation of U.S. Patent Application Serial No. 10/619,224, filed July 12, 2003; which is a continuation of U.S. Patent Application Serial No. 10/229,759, filed August 28, 2002, now Patent No. 6,733,977; which in turn is a continuation of U.S. Patent Application Serial No. 10/046,623, filed January 14, 2002, now Patent No. 6,551,817; which in turn is a continuation of U.S. Patent Application Serial No. 09/907,196, filed July 17, 2001, now Patent No. 6,399,365; which in turn is a continuation of U.S. Patent Application Serial No. 09/302,052, filed April 29, 1999, now Patent No. 6,287,850; which in turn is a continuation of U.S. Patent Application Serial No. 08/485,452, filed June 7,1995, now Patent No. 5,945,334; which is a

10/789,678 - 45 -

continuation in part of U.S. Patent Serial Application Serial No. 08/255,682, filed June 8, 1994.

Therefore, the '682 application is believed to constitute Applicants' earliest constructive

reduction to practice of an embodiment within the scope of the interfering subject matter.

In accordance with 37 C.F.R. § 41.202(a)(6), Applicant's provide a claim chart in

Appendix C showing that the '682 application provides a constructive reduction to practice of an

embodiment within the scope of the interfering subject matter. A courtesy copy of the '682

application is provided with this Request as Appendix D.

VII. Conclusion

In view of the above, Applicants respectfully request the Examiner to advance this case

to the Board of Patent Appeals and Interferences for the declaration of an interference between

Applicants' present application and the '702 patent. Applicants respectfully request that the

Examiner handles this matter on an expedited basis.

Respectfully submitted,

AFFYMETRIX, INC.

Date: May 2, 2005

Rhilip L. McGarrigle

Rěg. No. 31,395

Affymetrix, Inc. Legal Department 3380 Central Expressway Santa Clara, CA 95051 (408) 731-5000 (phone)

(408) 731-5392 (fax)

INTERFERENCE INITIAL MEMORANDUM

Count #____

To the Board of Patent Appeals and Interferences:

An interference is proposed involving the following ____ parties

 PARTY
 APPLICATION NO.
 FILING DATE
 PATENT NO., IF ANY
 ISSUE DATE, IF ANY

 Junior Party
 09/938,909
 08/24/2001
 6,682,702
 01/27/2004

If the involved is a patent, have its maintenance fees been paid? Yes _____ No ____Not due yet _____

Proposed priority benefit (list all intervening applications necessary for continuity):

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
USA	09/938,909	08/24/2001	6,682,702	01/27/2004
The claim(s) of this party corr 1-49	responding to this count:			
PATENTED OR PATENTABLE PENDING CLAIMS		UNPATENTABLE PENDING CLAIMS		
Patented claims 1-49			None	
The claim(s) of this party NO None	T corresponding to this count:		,	

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Senior Party Besemer et al.	10/789,678	02/27/2004	N/A	ˆγ. N/A

If the involved is a patent, have its maintenance fees been paid? Yes ____ No ___ Not due yet X

Proposed priority benefit (list all intervening applications necessary for continuity):

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
USA	10/619,224	07/12/2003	N/A	
USA	10/229,759	08/28/2002	6,733,977	05/11/2004
USA	10/046,623	01/14/2002	6,551,817	04/22/2003
USA	09/907,196	07/17/2001	6,399,365	06/04/2002
USA	09/302,052	04/29/1999	6,287,850	09/11/2001
USA	08/485,452	06/07/1995	5,945,334	08/31/1999
USA	08/255,682	06/08/1994	N/A	

The claim(s) of this party corresponding to this count:

141-163

PATENTED OR PATENTABLE PENDING CLAIMS		UNPATENTABLE PENDING CLAIMS		
Patentable pending claims 141-163		N/A		
The claim(s) of this party N None	OT corresponding to this count:			
 (Check off each step, if applicable) INSTRUCTIONS 1. Obtain all files listed above. 2. Confirm that the proposed involved claims are still active and all corrections and entered amendments have been considered. The patents must not be expired for, among other things, failure to pay a maintenance fee (Check PALM screen 2970). 3. If one of the involved files is a published application or a patent, check for compliance with 35 U.S.C. 135(b). 4. Obtain a certified copy of any foreign benefit documents where necessary (37 CFR 1.55(a)). 5. Discuss the proposed interference with an Interference Practice Specialist in your Technology Center. 				
DATE	PRIMARY EXAMINER (signature)	ART UNIT	TELEPHONE NUMBER	

INTERFERENCE PRACTICE SPECIALIST or TECHNOLOGY CENTER DIRECTOR (signature)

DATE

TELEPHONE NUMBER